To: Beck, Nancy[Beck.Nancy@epa.gov]
Cc: Bahadori, Tina[Bahadori.Tina@epa.gov]; Yamada, Richard (Yujiro)[yamada.richard@epa.gov]; Morris, Jeff[Morris.Jeff@epa.gov]
From: Thayer, Kris
Sent: Wed 9/13/2017 8:11:02 AM
Subject: RE: IRIS Materials for the 27-28 September SAB-CAAC meeting

Thanks for the questions Nancy – I've added some brief comments below. Some of these points are probably best discussed in real-time. We are swamped until after the September SAB CAAC but perhaps we can find time to meet in October?

From: Beck, Nancy
Sent: Tuesday, September 12, 2017 9:37 PM
To: Thayer, Kris <thayer.kris@epa.gov>
Cc: Bahadori, Tina <Bahadori.Tina@epa.gov>; Yamada, Richard (Yujiro) <yamada.richard@epa.gov>; Morris, Jeff <Morris.Jeff@epa.gov>
Subject: RE: IRIS Materials for the 27-28 September SAB-CAAC meeting

Kris,

Thanks for sharing. I've only skimmed the documents very quickly but I do have a few simple questions:

•□□□□□□□ Its still not clear to me what you mean by a portfolio approach. Is it that you may simply do a RfC before or separate from a RfD or cancer value? That's just one example of the portfolio. Is the basic framework for developing each endpoint going to remain the same and will you continue to use the RfV's and the cancer values as the endpoints of interest? It isn't clear to me how this moves us away from "one size fits all." For instance in OPPT we rely on a POD and don't apply UF's as IRIS does, so we don't really need IRIS to develop RfV's for us. We are fine to provide OPPT with PODs only, but we should discuss how this will best work in practice, in particular for assessments where OPPT isn't the only EPA Office/Program with an interest in the assessment. Tina and I have some options in mind and would welcome the opportunity to discuss.

•□□□□□□□ In your attachment A figure for the IAP, it would be useful to explain to us where you plan to have internal EPA review. After which steps? The draft IAPs went through internal agency review over the summer. Beyond the draft IAP stage, we are working within the existing internal EPA review processes. We have a slide on this for the upcoming September 20 STPC meeting.

•□□□□□□□ While the scoping summary table shows what programs may have an interest in a value, where can we find information on how IRIS prioritizes which chemicals to review? Is

IRIS planning to do a prioritization exercise anytime soon within the Agency? For example, there are 189 HAPs and not many of them have IRIS values, how will you decide which HAPs to review? It seems the need for them would be consistent under 112d. This is a good topic for a fuller discussion but in short, our prioritization is based on standing commitments (such as multi-year agenda chemicals – but confirming they meet current administration priorities), finding capacity to meet emerging needs of the agency (especially for small evidence-base topics), and staff resources.

•□□□□□□□ I'm not sure tables/visuals that show the number of studies available for each endpoint are on their own useful. Doesn't the quality of those studies matter? Is this just a screening tool to help focus the evaluation? Yes, the number of study inventories are used as a screening tool to help us get a sense of level of effort, nature of the evidence (e.g., epi, animal, in vitro), and type of expertise that will likely be required to conduct the assessment

•□□□□□□□ In the specific aims, looking at EB as an example, it says you will evaluate risk of bias and sensitivity. How does this evaluation compare to something like the ToxRTool which is used internationally (or Klimisch which was used quite a bit by OPPT for our HPV program), to evaluate the study quality of toxicological data? This is probably a good topic for a briefing, but in short the IRIS approach includes a reporting quality domain that covers much of the ToxRTool content, but also has other domains that are more widely used in the SR community. Applicability or relevance of the study to the assessment question can be addressed as part of adherence to the PECO-statement. Obviously, we save resources if we don't spend time doing study quality assessment or data extraction on studies that are not really relevant to the assessment needs. We also consider applicability as part of our structured framework for assessing weight of evidence. Consistent with standards in systematic review, we do try to be transparent in separating out considerations related to risk of bias (internal validity) and applicability.

•□□□□□□□ You note that studies with critical deficiencies will be considered uninformative, but what about other gradations of study quality? The discussion on synthesis makes no mention of giving preference to higher quality studies over lower quality studies. This is important to us as TSCA requires us to consider quality when integrating information. Again, a good topic of a briefing. We explicitly consider the other gradations of study quality as part of our evidence synthesis, which we are trying to make more consistent and transparent via use of evidence profile tables. I think for future draft IAPs we can consider elaborating on that specific aim to give the reader a sense of factors we consider during the process of evidence synthesis. A fuller description of the evidence synthesis process is presented in chemical-specific protocols and the IRIS Handbook.

•□□□□□□□ In the PECO statement, looking at EB, under exposure, there really doesn't seem to be any consideration of environmentally relevant doses. Is IRIS continuing to focus on any dose from animal studies and mechanistic studies without trying to give a preference to doses that may be within the range of typical human exposures. It really depends on the Agency scoping need and also the chemical in question. For example, if the Agency scoping need isn't already targeted to a certain dose range, then we may need to consider the size and nature of the evidence base during our initial problem formulation….e.g., when there are a lot of studies then

we may opt to focus on those that test lower doses….or perhaps limit the SR to focus to health outcomes that are associated with lower dose effects. I'm very curious how you are approaching this for TSCA, in particular as you move into full-text review screening criteria and subsequent implementation of SR.

Thanks again for sharing the documents.

Nancy

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From: Thayer, Kris
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Subject: FW: IRIS Materials for the 27-28 September SAB-CAAC meeting

Nancy,

Good morning. Please find attached the draft IRIS Assessment Plans (IAPs) for the upcoming SAB CAAC meeting (September 27-28). For context, the draft IAPs do NOT represent the last public outreach during the course of preparing a draft assessment. During the September meeting, we will spend a significant amount of time discussing additional transparency steps in IRIS process for implementing SR.

We are happy to tell you more about our processes if you'd like. During our previous meetings, we really focused on *how* we are implementing SR within IRIS (e.g., methods) but we have not yet shared with you approaches for making it pragmatic or steps for promoting transparency during the course of the assessment.

Please let us know if you have any questions or would like to meet and discuss,

Kris

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Subject: IRIS Materials for the 27-28 September SAB-CAAC meeting

Hello Everyone,

Attached, you will find the IRIS background documents for the upcoming SAB Chemical Assessment Advisory Committee (SAB-CAAC), scheduled for 27-28 September. The "IAP Background" provides an overview of the expectations for this meeting. The other three documents are IRIS Assessment Plans (for nitrate/nitrite, chloroform, and ethylbenzene) that demonstrate how systematic review is being formally integrated into the existing scoping and problem formulation step of IRIS. Many of you were involved in and helped in shaping these efforts over the past few months – and we thank you! More information about the SAB meeting can be found:
https://yosemite.epa.gov/sab/sabproduct.nsf//MeetingCalBOARD/B993D2C54053CD9A8525817D005FD1E2?

Please let us know if you have any questions or need additional information.

Tina

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